In Vivo Imaging of Human Embryonic Stem Cell Derivatives and Tumorigenicity

Grant Award Details

In Vivo Imaging of Human Embryonic Stem Cell Derivatives and Tumorigenicity

Grant Type: SEED Grant

Grant Number: RS1-00322

Investigator:

Name:	Joseph Wu
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $623,634

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: In Vivo Imaging of Human Embryonic Stem Cell Derivatives and Tumorigenicity

Public Abstract:

Human embryonic stem cells (hESCs) are one of the most fascinating subjects of interest in all of biology and medicine these days. Under certain physiologic conditions, they can be induced to become specialized cells such as brain, cardiac, liver, pancreatic, and bone marrow cells. This opens up the exciting possibility that hESCs may one day be used to treat patients with Parkinson's disease, heart conditions, hepatitis, diabetes, and leukemia, just to name a few currently intractable diseases that affect millions of Americans alone. This field of cell-based therapies to treat human diseases is generally referred to as "regenerative medicine."

Scientists who want to study hESCs or their specialized cell derivatives typically inject them into small animal models such as mice and rodents. However, researchers currently are unable to monitor noninvasively these cells after transplant. Instead, these animals are typically sacrificed for postmortem biopsy, which precludes long-term follow-up of transplanted cells. Without the ability to follow the progress of transplanted cells over a longer period of time, important insights into hESC fates in vivo have not been forthcoming. Thus, developing a novel technology to track transplanted hESCs and their specialized cell derivatives would represent a major advancement in this field that will produce wide-ranging theoretical and practical implications.

Another problem with transplantation of hESCs is the potential to cause teratomas. Teratomas are disorganized arrays of cell differentiation that appear to recapitulate many of the events involved in early embryonic development. Clearly, the teratoma formation risk is a major obstacle to future clinical application of hESCs. In this proposal, we will evaluate how teratoma forms in living subjects over time using the imaging techniques that we have developed as well as how best to prevent them in the first place.

Due to the serious risks posed by teratoma formation, it is necessary to induce hESCs to become specialized cell derivatives first before transplantation for therapeutic purposes. However, this process is not efficient at present despite intense efforts searching for methods to expedite it. Our team plans to tackle this problem using the latest genomics and proteomics technology.

In summary, our proposal is a targeted response to the CIRM SEED grant. It seeks to develop a novel technology (molecular imaging) that will address a critical barrier in clinical translation of hESC therapy (teratoma formation) and provide a better understanding of cardiac cell differentiation process (genomics/proteomics). Our well-established multidisciplinary team has the required training, experience, and innovation to complete the project. Overall, we are confident that our proposed studies will generate significant progress in this field, in both scientific knowledge and useful therapies.

Statement of Benefit to California:

Stem cell based therapy holds great promise for treatment of numerous diseases. Human embryonic stem cells (hESCs), for example, can transform into brain, cardiac, pancreatic, liver, and bone marrow cells. This opens up the exciting possibility that hESCs may one day be used to treat diseases such as Parkinson's, heart conditions, hepatitis, diabetes, and leukemia. This field of cell-based therapies to treat human diseases is generally referred to as "regenerative medicine."

However, we are still at the very early stages of understanding the capability of hESCs. There are many basic research questions that need to be addressed before we can begin clinical trials involving specialized hESC-derived cells in the future. For example, we need to understand how to drive hESC differentiation into specific pathways, to control hESC proliferation, and to monitor their cell fate after transplantation.

One of the most serious problems is the potential for hESC to cause teratoma after transplantation. Teratomas are benign tumors that consist of cells from different lineages. Therefore, it is critical for scientists to understand how teratomas are formed as well as to develop techniques to monitor them noninvasively and repetitively. Our research proposal is designed to address all 3 questions: (1) how to image and monitor transplanted hESCs, (2) how teratomas are formed, and (3) how to reliably induce hESCs to become specialized derivatives such as cardiac cells.

We believe that answering these questions will lead to significant advances in hESC research and novel therapies. We have assembled a multidisciplinary team of experienced investigators to attack the challenges of this project. At the same time, we will train and mentor a new generation of bright students and junior scientists in the areas of technology development and hESC biology. This ensures that an essential knowledge base will be preserved and passed on for the foreseeable future.
